DECLARATION OF GILBERT R. GONZALES

[0001] I, Gilbert R. Gonzales, hereby state and declare the following:

[0002] I am a named inventor on the present application, U.S. Serial No. 10/675,147 ("the '147 Application"), which is assigned to Serene Medical, Inc. of New York, New York. I have B.Sc. (1973) and M.D. (1977) degrees from the University of Arizona. I have performed research in the area of pain, including methods for treating pain by delivery of medications to the intraspinal area via the vertebral venous system, otherwise referred to as Batson's plexus.

[0003] In addition to my research, I belong to the following scientific and medical societies: American Academy of Neurology (Facilitator, Physical Treatments of Chronic Pain, American Academy of Neurology Therapeutics and Technology and Assessment Subcommittee, May, 1992-1996; Member, American Academy of Neurology Continuum Committee on Pain, Kenneth Casey, Facilitator, March, 1994); American Pain Society; Eastern Pain Society; International Association for the Study of Pain; and the Western Pain Society.

[0004] I have also served on the following Editorial Boards: American Pain Society Journal, 1993 (ad hoc reviewer); Journal of Pain and Symptom Management, 1993-present (ad hoc reviewer); The Pain Medicine Journal Club Journal, 1994 - expert analyst; Pain Forum, 1999 (ad hoc reviewer); and The Clinical Journal of Pain, 2000 (ad hoc reviewer).

[0005] Additionally, I have held the following positions and appointments: Assistant Professor of Neurology, 1990-1992, Department of Neurology, University of Cincinnati School of Medicine, Cincinnati, Ohio; Assistant Professor of Neurology, 1992-1998 and

Associate Professor of Neurology, 1998, Mayo Medical School; Vice Chairman, Department of Neurology, 1994-1998, Mayo Clinic, Scottsdale, Arizona; Assistant Adjunct Professor, 1997-1998, Department of Psychology, University of New Orleans, New Orleans, Louisiana; Associate Attending Neurologist, 1998-2002, Memorial Hospital for Cancer and Allied Diseases, New York, New York; and Associate Member, 1998-2002, Memorial Sloan-Kettering Cancer Center, New York, New York.

[0006] Further, to my knowledge, since the work of Oscar Batson (who first described Batson's plexus and after whom the plexus is named), I am the only person who has consistently researched delivery of pain medications into the intraspinal region using reversal of blood flow in Batson's plexus. To my knowledge, I am the only individual who has published in this area and who has been a named inventor on patents and patent applications in this area. As such, in my view, I am the only person skilled in the area of delivery of pain medications into the intraspinal region via reversal of blood flow in Batson's plexus.

[0007] I have reviewed the references cited against the claims of the '147 Application, including U.S. Patent Nos. 5,846,216 (Gonzales), 4,941,875 (Brennan), and 5,061,243 (Winchell). I am a named inventor on Gonzales. Gonzales describes a system for rectal administration of medication into a patient body. Medication is dispensed through a delivery tube and to a dispenser head positioned in the rectum of a patient. When delivered rectally, as in Gonzales, medication is transported across the rectal mucous membranes and then into the patient's vasculature. The medication thus cannot be directed to a particular vein, but rather enters many veins. Once within the patient's vasculature and/or during delivery to the vasculature, an abdominal restraint or

binder may be used to increase abdominal pressure to reverse blood flow in Batson's plexus, thereby delivering some medication into the intraspinal area.

[0008] In the present '147 Application, I have now developed a system for administering medications by catheterization (or use of a needle or other delivery component) of the pudic vein, the internal pudic vein, or the external pudic vein (the "pudic family of veins"). Thus, medication can now be directly administered to a patient's intraspinal area via veins that directly communicate with Batson's plexus (to the exclusion of cross-communication with any other vascular region, as occurs when using the rectal dispenser head of Gonzales). However, until the claimed invention of the '147 Application, medication was not directly administered via veins that directly communicate with Batson's plexus. Indeed, until I developed the claimed invention of the '147 Application, medication could not have been administered via veins that directly communicate with Batson's plexus. And so, until the claimed invention of the '147 Application, rectal administration (as described in Gonzales) was the only sort of administration that could be used to direct drugs into a patient's vasculature to be subjected to reversal of blood flow in Batson's plexus.

[0009] In the present Office Action (dated April 16, 2007), the Examiner suggests that the claimed infusor system and method of administering medications would have been obvious over Gonzales in view of Brennan or Winchell. In particular, upon the background of rectal mucous membrane delivery taught by Gonzales (as described above), the Examiner uses Brennan or Winchell for their teaching of drug delivery via a venous needle. Brennan and Winchell show standard IV setups for controlled continuous delivery of drug via peripheral venous delivery. The Examiner suggests that

replacing the rectal delivery head of Gonzales with IV administration, as shown in Brennan or Winchell, would have been obvious to one skilled in the art.

[0010] In particular, the Examiner states, "The advantages of utilizing direct delivery via a needle/catheter rather than going through a membrane are well known in the art." This may be true in the standard venous system, but it is not true in Batson's plexus, which is one of many venous plexuses and one of the few true isolated plexuses of the body (the others being the plexus around the esophagus, and the plexus that includes the interior carotid for the eye). First, the plexuses are often very poorly anatomically defined. And so, the vessels that comprise the plexus or communicate with the plexus are also poorly defined. Second, the plexus is variable from person to person in terms of the veins that comprise the plexus or communicate with the plexus (i.e., vein "X" may communicate with Batson's plexus in patient "A," but not in patient "B"). So, until I developed the claimed invention, no one knew, in an individual human, how many and which veins, if any, were actually useful for delivering medication via Batson's plexus. This problem, however, does not present itself with the rectal mucous membrane delivery of Gonzales, since medication that is transported across the rectal mucous membranes cross-communicates with all veins in the region, thereby resulting in medication being delivered to the intraspinal region in any patient in which it is tried.

[0011] And so, with such direct venous delivery thought to be impossible, I did not include it in Gonzales (again, because I did not know, nor did anyone know, that there were veins that communicated with and allowed delivery to the intraspinal region via reversal of Batson's plexus). And again, no one knew this until I determined and described the direct communication of veins in the present '147 Application. Thus, even

though the teachings of Gonzales, Brennan, and Winchell were known, that knowledge would have been useless to anyone who wanted to deliver medication in Batson's plexus via direct vein delivery. In other words, even if one were to replace the rectal dispenser head with a catheter (or needle, or other delivery component), one still could not deliver medications to the intraspinal region because that individual would not know where to insert the catheter. Thus, an individual skilled in the art, and armed with the knowledge of the cited references, would not replace the rectal dispenser head of Gonzales because to do so would result in no medication reaching the intraspinal region, whereas the dispenser head would result in medication reaching the intraspinal region. As such, at the time, there were no advantages in utilizing direct delivery via a needle/catheter rather than going through a membrane. Quite the contrary, utilizing direct delivery via a needle/catheter would have been disadvantageous.

[0012] In fact, if such a change was so advantageous, why was it not done before the presently claimed invention (especially given the numerous advantages that would obtain through direct vein catheterization)? In 1940, Oscar Batson first described the plexus, and taught that the dorsal vein of the penis could communicate with the plexus. However, Batson taught that the dorsal vein of the penis was the only vein that could allow such delivery. From 1940 until the '147 Application, there had only been one other study that elucidated a vein that could communicate with Batson's plexus. That study was performed by me, and determined that the dorsal vein of the tail in rats communicated with the plexus. However, neither of these two veins is useful in delivering medication in humans. First, humans do not have a dorsal vein of the tail (since humans do not have a tail). Second, any attempted delivery of drug via the

dorsal vein of the penis is not feasible, especially in the non-erectile penis, and such delivery is not possible in women.

[0013] Thus, from 1940 (when Batson first described the plexus) until my work, which resulted in the '147 Application being filed in 2003, nobody could deliver medication into the intraspinal region via direct vein catheterization and using the reversal of blood flow in Batson's plexus (a span of 63 years). So, until I actually discovered the communication of the particular veins with Batson's plexus recited in the present claims, no one had, or would have had, any idea that venous delivery would work or could work. If Batson or others after him (although there have been none until me, and until the presently claimed invention) could have anticipated another venous route other than the dorsal vein of the penis, I believe that it would have been tried and/or used by Batson and many other anatomists/surgeons due to the many advantages that would obtain.

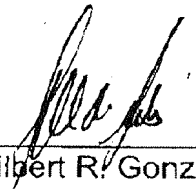
[0014] For example, catheterization of the pudic family of veins allows the patient to be upright and ambulatory during the dispensing of medication. This contrasts with the rectal dispenser head mucous membrane infusion of Gonzales, wherein a patient must remain recumbent during the dispensing of medication. Further, previous drugs that could not be infused rectally (for example, those with structure too large to cross the rectal mucous membranes) can now be administered by delivery via the pudic family of veins. Further, massive drug deliveries can be given through catheterization of the pudic family of veins. The rectal dispenser head mucous membrane infusion method exhibits an across-the-membrane rate limiting effect, which requires relatively potent drugs to be delivered (due to the relatively low volume per time of infusion). However,

through a system including IV delivery via the pudic family of veins, one can deliver high volumes of low potency drugs. And further, because the pudic family of veins directly communicates with Batson's plexus (to the exclusion of any cross-communication with other vessels), medications may be delivered directly to Batson's plexus without the medication being diluted by diversion to other vessels. In the previous rectal dispenser head mucous membrane infusion of Gonzales, drugs could not be focused to particular veins (such as the pudic family of veins), and thus would also enter vessels having cross-communication with other vessels of the body. Given all these advantages, it is my opinion that if catheterization of the pudic family of veins, and thus IV delivery of medication to the intraspinal region via reversal of blood flow in Batson's plexus were obvious, it certainly would have been done previously.

[0015] I hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Further Declarant sayeth naught.

July 13, 2007
Date



Gilbert R. Gonzales